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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,946	08/09/2005	Bernard Pau	263432US0XPCT	4965

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
05/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/516,946	PAU ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-13,19-24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *6,7,9,13 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,8,10-12,24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/07 has been entered.

Claims 26-27 have been added by Applicant.

Claims 1, 2, 5-13, 19-24, 26, and 27 are pending.

Claims 6, 7, 9, 13, and 19-23 are withdrawn.

Claims 1, 2, 5, 8, 10-12, 24, 26, and 27 are currently under consideration.

The following Office Action contains New Rejections.

Objections Withdrawn

All previous objections are withdrawn.

Rejections Withdrawn

All previous rejections are withdrawn.

New Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 26 is rejected under 35 U.S.C. 102(a) as being anticipated by Macpherson et al (Proceedings of the American Association for Cancer Research Annual Meeting, 3/02, 43:407-408).

Claim 26 is broadly drawn to a process for detecting resistance of a cancer cell to oxaliplatin treatment comprising: detecting the level of mitochondrial apoptosis in a cancer cell from a subject having cancer and in a control cell not resistant to Oxaliplatin, wherein a lower level of mitochondrial apoptosis in said cancer cell compared to the control cell is indicative of oxaliplatin resistance.

Macpherson et al teaches a process for detecting resistance of a cancer cell to oxaliplatin treatment comprising: detecting the level of mitochondrial apoptosis in a cancer cell (cells with bcl–xl) from a subject having cancer and in a control cell not resistant to Oxaliplatin (bcl-xl ko cells), wherein a lower level of mitochondrial apoptosis in said cancer cell compared to the control cell is indicative of oxaliplatin resistance (see abstract, in particular).

Claim 26 is rejected under 35 U.S.C. 102(a) as being anticipated by Arango et al et al (Proceedings of the American Association for Cancer Research Annual Meeting, 3/02, 43:457).

Arango et al teaches a process for detecting resistance of a cancer cell to oxaliplatin treatment comprising: detecting the level of mitochondrial apoptosis, which is characterized by a dissipation of the mitochondrial membrane potential and caspase-3 activation, in cancer cells from subjects having cancer and in a control cell not resistant to Oxaliplatin (wild-type P53 cells), wherein a lower level of mitochondrial apoptosis in said cancer cell compared to the control cell is indicative of oxaliplatin resistance (see abstract, in particular).

Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Fink et al (Cancer Research, November 1996, 56:4881-4886), as evidenced by Arango et al et al (Proceedings of the American Association for Cancer Research Annual Meeting, 3/02, 43:457).

Fink et al teaches a process for detecting resistance of a cancer cell to oxaliplatin treatment comprising: detecting the level of apoptosis, which Arango et al evidences is mitochondrial apoptosis, in cancer cells from subjects having cancer and in a control cell not resistant to Oxaliplatin, wherein a lower level of mitochondrial apoptosis in said cancer cell compared to the control cell is indicative of oxaliplatin resistance (see Figure 2, in particular).

Claims 1, 2, 5, 10, 12, 24, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Maurer et al (Digestive Diseases and Sciences, 43(12): 2641-2648).

Claim 1 is drawn to a process comprising detecting expression of an effector or marker gene expressing the pro-apoptotic Bax protein in a cancer cell. Claim 2 is drawn to the process of claim 1 wherein the cancer cell is selected from a group consisting of a cell obtained from a subject having colorectal cancer. Claim 5 is drawn to process of claim 1, comprising detecting mRNA transcripts of said effector or marker gene. Claim 10 is drawn to the process of claim 1, wherein a probe or primer is used to detect the expression of said effector or marker gene. Claim 12 is drawn to the process according to claim 1, comprising contacting a nucleotide probe for said effector or marker gene with a biological sample to be analyzed for a time and under conditions suitable for hybridization to occur, and detecting hybridization. Claim 24 is drawn to the process of claim 1, wherein said cancer cell is a colorectal cancer cell and said detecting comprises detecting the level of expression of mRNA encoding Bax. Claim 27 is drawn to a process comprising measuring the level of mRNA encoding Bax.

It is noted that the preambles of the instant claims are about intended purposes of the claimed methods, and the "wherein" clauses are not active method steps. Therefore, the preambles and the "wherein" clauses are not considered limitations to the claims.

Maurer et al teaches a process comprising measuring the level of mRNA encoding Bax by detecting expression of an effector or marker gene expressing the pro-apoptotic Bax protein in a colorectal cancer cell from a subject having colorectal cancer,

comprising detecting mRNA transcripts, wherein a probe or primer is used to detect the expression of the Bax gene, comprising contacting a nucleotide probe for said effector or marker gene with a biological sample to be analyzed for a time and under conditions suitable for hybridization to occur and detecting hybridization (see Figure 2, in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurer et al (Digestive Diseases and Sciences, 43(12): 2641-2648) as applied to claim

1 above, and further in view of Aggarwal et al (J Immunol, February 1998, 160(4): 1627-1637).

The teaching of claim 1 by Maurer et al is discussed above.

Maurer et al does not specifically teach the process of claim 1 comprising obtaining a cDNA from the RNA of the biological sample and amplifying the cDNA using at least one primer for amplification of BAX. However, this deficiency is made up in the teachings of Aggarwal et al.

Aggarwal et al teaches a quantitative PCR method comprising obtaining a cDNA from RNA of a biological sample and amplifying the cDNA using at least one primer for amplification of BAX (Figure 7, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use a quantitative PCR method comprising obtaining a cDNA from RNA of a biological sample and amplifying the cDNA using at least one primer for amplification of BAX when detecting the expression of BAX in the method of Maurer et al because the quantitative PCR method of Aggarwal et al would provide quantitative results for determining BAX expression in the method of Maurer et al . One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using a quantitative PCR method comprising obtaining a cDNA from RNA of a biological sample and amplifying the cDNA using at least one primer for amplification of BAX when detecting the expression of BAX in the method of Maurer et al because Aggarwal et al teaches primers that amplify BAX cDNA and methods of using said primers to amplify BAX cDNA (page 1628, in particular).

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claims 1, 2, 5, 8, 10, 12, 24, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurer et al (Digestive Diseases and Sciences, 43(12): 2641-2648) as applied to claims 1, 2, 5, 10, 12, 24, and 27 above, and further in view of Macpherson et al (Proceedings of the American Association for Cancer Research Annual Meeting, 3/02, 43:407-408) and Chao et al (J Exp Med, September 1995, 182(3): 821-828).

Teaching of claims 1, 2, 5, 10, 12, 24, and 27 by Maurer et al is discussed above. Maurer et al also teaches expression of the BAX gene varies in colorectal cancer cells (see Figure 2, in particular).

Maurer et al does not specifically teach methods comprising determining the level of expression of BAX gene in cancer cells obtained from a patient and comparing the level with the level measured in a corresponding control sample of cells not resistant to oxaliplatin. However, these deficiencies are made up in the teachings of Macpherson et al and Chao et al.

Macpherson et al teaches reduced expression of Bcl-xl in colon cancer cells results in an enhanced apoptotic response to oxaliplatin (see abstract).

Chao et al teaches Bcl-xl functions as a repressor of apoptosis by heterodimerizing with and inhibiting pro-apoptotic BAX (page 821 and page 826, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to perform a method of detecting resistance of a cancer cell to oxaliplatin treatment by determine the level of expression of BAX gene in cancer cells obtained from the patient and comparing the level with the level measured in a corresponding control sample of cells not resistant to oxaliplatin when performing the method of Maurer et al because Macpherson et al teaches reduced expression of Bcl-xl, a repressor of apoptosis that functions by inhibiting BAX (see pages 821 and 826 of Chao et al), in colon cancer cells results in an enhanced apoptotic response to oxaliplatin (see abstract of Macpherson et al). Therefore, colorectal cancer cells with less BAX expression detected in the method of Maurer et al would be expected to be more resistant to oxaliplatin than cells with higher levels of BAX expression because apoptosis of colorectal cancer cells by oxaliplatin has been shown to be controlled by a Bcl-xl mediated pathway, the expression level of a member of the Bcl-xl mediated apoptotic pathway (Bcl-xl) has been shown to modulate the Bcl-xl mediated apoptotic pathway in colorectal cells in response to oxaliplatin, and BAX is a pro-apoptotic molecule that is repressed by Bcl-xl. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing a method of detecting resistance of a cancer cell to oxaliplatin treatment by determine the level of expression of BAX gene in cancer cells obtained from the patient and comparing the level with the level measured in a corresponding control sample of cells not resistant to oxaliplatin when performing the method of Maurer et al because Macpherson et al teaches reduced expression of Bcl-xl, a repressor of apoptosis that

functions by inhibiting BAX (see pages 821 and 826 of Chao et al), in colon cancer cells results in an enhanced apoptotic response to oxaliplatin (see abstract of Macpherson et al). Therefore, colorectal cancer cells with less BAX expression detected in the method of Maurer et al would be expected to be more resistant to oxaliplatin than cells with higher levels of BAX expression because apoptosis of colorectal cancer cells by oxaliplatin has been shown to be controlled by a Bcl-xl mediated pathway, the expression level of a member of the Bcl-xl mediated apoptotic pathway (Bcl-xl) has been shown to modulate the Bcl-xl mediated apoptotic pathway in colorectal cells in response to oxaliplatin, and BAX is a pro-apoptotic molecule that is repressed by Bcl-xl. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642